Clinical Edit Criteria Proposal

Drug/Drug Class: **DMARDs Clinical Edit**

Prepared for: **Missouri Medicaid**
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☐ **New Criteria** ☒ **Revision of Existing Criteria**

Executive Summary

Purpose: Require evidence of treatment with oral methotrexate for rheumatoid arthritis before initiating leflunomide, auranofin, anakinra, etanercept, infliximab, or adalimumab therapy.

Why was this Issue Selected: Oral methotrexate therapy is effective in the treatment of rheumatoid arthritis. Leflunomide (Arava), Auranofin (Ridaura), Anakinra (Kineret), Etanercept (Enbrel), Infliximab (Remicade), and Adalimumab (Humira) therapies are significantly more expensive than methotrexate.

Program-specific information:

Drug	Claims	Expense
• Methotrexate, Oral	*45*	*$1,168*
• Leflunomide	*2,901*	*$766,793*
• Auranofin	*71*	*$8,676*
• Anakinra	*397*	*$320,554*
• Etanercept	*1,870*	*$1,949,917*
• Infliximab	*398*	*$1,033,569*
• Adalimumab	*33*	*$38,209*
	04/02 - 03/03	

Setting & Population: Prescribed in adult patients with Rheumatoid Arthritis.

Type of Criteria: ☐ **Increased risk of ADE** ☐ **Non-Preferred Agent** ☒ **Appropriate Indications** ☐

Data Sources: ☐ **Only administrative databases** ☒ **Databases + Prescriber-supplied**

Purpose of Clinical Edit Criteria

Under the Omnibus Budget Reconciliation Act of 1993, Congress intended Clinical Edit programs to control utilization of products that have very narrow indications or high abuse potential. While prescription expenditures are increasing at double-digit rates, payors are also evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. Clinical edit criteria assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class. Clinical edit criteria can also reduce the risk for adverse events associated with medications by identifying patients at increased risk due to diseases or medical conditions, or those in need of dosing modifications.

Why Has This Clinical Issue Been Selected For Review?

Rheumatoid arthritis (RA) is a chronic, disabling, autoimmune disorder estimated to affect approximately 1% of the population worldwide.[1] Disability caused by RA leads to significant economic consequences and reduced quality of life. The American College of Rheumatology Subcommittee on Rheumatoid Arthritis released updated guidelines in the spring of 2002.[2] The guidelines emphasize the need to start disease-modifying antirheumatic drug (DMARD) therapy early in the course of the disease, within three months of diagnosis if possible. DMARDs can prevent or reduce progressive joint damage, and traditionally have included methotrexate (MTX), sulfasalazine (SSZ), hydroxychloroquine (HCQ), azathioprine, D-penicillamine, oral or intramuscular gold, minocycline, cyclosporine, and more recently, leflunomide. The guidelines suggest using leflunomide (Arava®) as an alternative to MTX in patients who cannot tolerate MTX or who have had inadequate response to MTX. Time to benefit with the DMARDs is typically anywhere from one to six months, depending on the agent, and all have potential toxicities requiring monitoring. DMARD monotherapy is often not sufficient to prevent disease progression or control symptoms, and combination therapy is often required.

MTX is often the drug of first choice for RA based on efficacy, toxicity profile, and low cost. Additionally, MTX is generally a component of combination therapy regimens. Combination therapy regimens are being increasingly used as initial therapy in place of monotherapy. Triple therapy with MTX + HCQ + SSZ has demonstrated greater efficacy in meeting study endpoints than MTX, HCQ, or SSZ monotherapy, HCQ + SSZ, MTX + SSZ, or MTX + HCQ.[3-5] In general, dual therapy is more effective than monotherapy, and triple therapy is more effective than dual therapy.

In recent years several new agents have become available that target specific cytokines involved with inflammation in RA. The two cytokines currently targeted include tumor necrosis factor (TNF) and interleukin-1 (IL-1). As a group these DMARDs are often referred to as biologic agents. Of the available anti-TNF therapies, infliximab (Remicade®) and adalimumab (Humira®) bind to TNF-α, while etanercept (Enbrel®) binds to both TNF-α and TNF-β. Infliximab is currently only approved for use in combination with MTX for those patients who had an inadequate response to MTX,[6] etanercept is approved for use as monotherapy or in combination with MTX,[7] and adalimumab is approved for use as monotherapy or in combination with MTX or other DMARDs in patients who have not had an adequate response to one or more DMARDs.[8] Anakinra (Kineret®) is an IL-1 receptor antagonist that is approved for use in RA patients who have failed one or more DMARDs, and may be used as monotherapy or in combination with other DMARDs except TNF inhibitors.[9]

As a group the biologics have demonstrated improvement in signs and symptoms of RA, as well as demonstrating slowed rates of radiographic disease progression. A response is typically seen within days to a few weeks of starting these agents, as opposed to several months with most traditional DMARDs. Concerns with using the biologic agents include the need for long-term studies to verify safety (e.g., potential for serious infections or malignancies, given the role of these cytokines in host defense), parenteral administration, and high cost. The treatment algorithm in the American College of Rheumatology guidelines suggests potential use of biologic agents in patients with suboptimal response to MTX therapy.[2]

Setting & Population

- Drug class for review: Newer DMARD therapies
  adalimumab (Humira®)
  anakinra (Kineret®)
  etanercept (Enbrel®)
  infliximab (Remicade®)
  leflunomide (Arava®)
- Age range: Adult patients ≥ 18 years
- Gender: Male & female

Approval Criteria

- Diagnosis of rheumatoid arthritis with
  - Previous trial of methotrexate (past 720 days) OR
  - Contraindication to methotrexate therapy
- Etanercept only: Diagnosis of psoriatic arthritis, or ankylosis spondylosis
- Infliximab only: Diagnosis of Crohn's disease

Approval Diagnoses				
Condition	**Submitted ICD-9 Diagnoses**	**Inferred Drugs**	**Date Range**	**Client Approval (Initials)**
Rheumatoid Arthritis	714.0 – 714.8	--	720 days	
Psoriatic arthritis (etanercept only)	696.0		720 days	
Ankylosing Spondylitis (etanercept only)	720.0		720 days	
Crohn's disease (infliximab only)	555		720 days	
Contraindications to methotrexate use:				
Alcohol dependence/abuse	303 – 305.3	--	365 days	
Ascites	789.5	--	365 days	
Agranulocytosis	288.0	--	365 days	
Aplastic anemia	284.8	--	365 days	
Hypoplastic anemia	284.9	--	365 days	
Immunodeficiency	279	--	365 days	
HIV	042	--	365 days	
Liver disease	570-573	--	365 days	
Pleural effusion	511.1, 511.8, 511.9	--	365 days	
Renal impairment	580-588	--	365 days	
Thrombocytopenia	287.3 – 287.5	--	365 days	
Current pregnancy without delivery code	V22 – V239, 640 – 648	--	270 days	

Denial Criteria

- Absence of diagnosis for rheumatoid arthritis, or psoriatic arthritis (etanercept only), or ankylosing spondylosis (etanercept only) or Crohn's disease (infliximab only)
- No history of methotrexate use in the absence of contraindications to methotrexate therapy

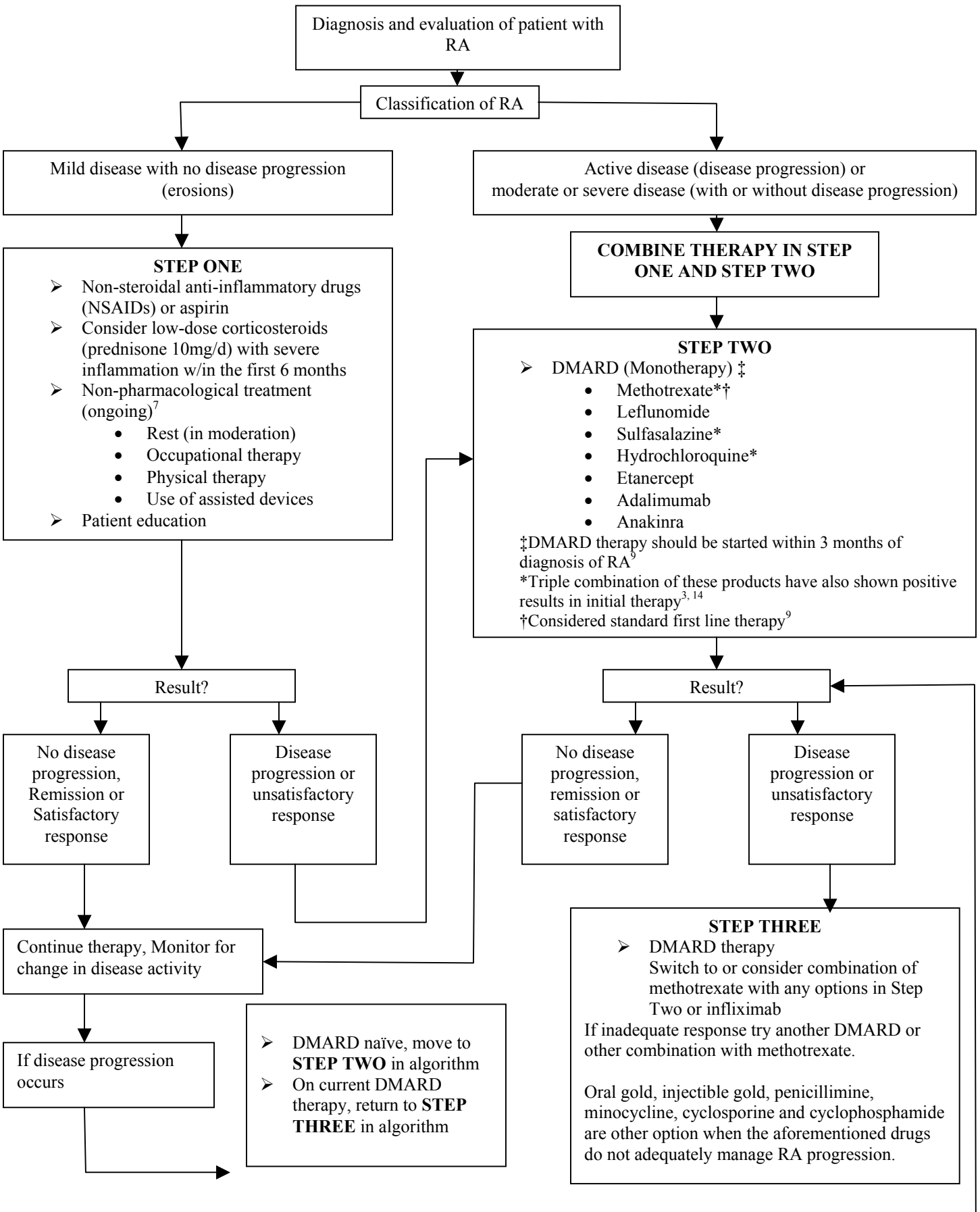
Required Documentation

Laboratory results: ☐ Progress notes: ☐
MedWatch form: ☐ Other: ☐

Disposition of Edit

- **Denial:** Exception 682 "Clinical Edit"

Rheumatoid Arthritis Algorithm



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